REMARKS

1. PRELIMINARY

With the amendment submitted herewith, claims 1-3, 5 and 7 are pending in the application. Claims 4 and 6 and 8-36 are canceled in view of the Restriction Requirement mailed January 28, 2002 and the Office Action mailed August 6, 2002. Claim 1 is the only independent claim under examination and is amended herewith. Support for the amendment may be found in the specification as originally filed. More specifically, support may be found in the claims as originally filed.

2. PRIORITY CLAIM

The Office Action states that the claimed subject matter of the instant claim 7 is given priority only to the filing date of the instant application (March 26, 2001) for SEQ ID NOS:17 and 18. The Office Action requests that Applicants clarify by Affidavit or Declaration that the instantly disclosed and claimed SEQ ID NOS:17 and 18 are the same sequences as MG2608, MG2725, AS1 or MM in the figures the provisional applications to which the instant application claims priority (60/192,157 and 60/261,522).

Applicants hereby declare that SEQ ID NO:17 of the instant application is identical to MG2608 and SEQ ID NO:18 is identical to MG2607, both of which are disclosed on page 18, Table 1, of U.S. Serial No. 60/192,157 (filed March 24, 2000). Applicants assert their right to priority for SEQ ID NOS: 17 and 18 for the earliest priority date to which the instant application claims priority. Applicants do not believe that a formal Affidavit or Declaration is warranted, as review of Table 1 of Serial No. 60/192,157 makes the accuracy of this statement clear.

3. INFORMATION DISCLOSURE STATEMENT

Applicants acknowledge the statement regarding the Information Disclosure Statement filed on April 4, 2002. More specifically, the Office Action states that with the exception of reference C10 under "Other Documents", the Information Disclosure Statement is acceptable.

Reference C10 is the International Search Report of PCT/US01/09651. Applicants provided copies of all references cited in the International Search Report (C10) with the Supplemental Information Disclosure Statement filed April 4, 2002, with the exception of Yoshida et al. (1990) "Potent and Specific Inhibition of Mammalian Histone Deacetylase Both In Vivo and In Vitro By Thrichostatin A," 265(28) *J. Biol. Chem.* 17174-17179. Yoshida et al. was cited in the Information Disclosure Statement filed October 1, 2001 as Reference A1, and a copy was provided therewith. Copies of initialed PTO 1449 forms dated July 28, 2002 are enclosed for the Examiner's reference.

4. CLAIM OBJECTIONS

Applicants acknowledge the objection to claim 6 in view of the Restriction Requirement. Because claim 6 and claim 1 as examined are drawn to the same subject matter, Applicants have requested the cancellation of claim 6 with the amendment submitted herewith.

5. REJECTIONS

A) Rejection of Claims 1-7 Under the Doctrine of Obviousness-Type Double Patenting

Claims 1-7 stand rejected under the doctrine of Obviousness-Type Double Patenting as being unpatentable over claims 1-11 of copending Application No. 09/817,913.

Applicants defer the filing of a Terminal Disclaimer until such time that claims in one or the other applications are otherwise found allowable.

B) Rejection of Claims 1 and 6 Under 35 U.S.C. § 102(b) or in the alternative Under 35 U.S.C. § 103(a) in view of WO 89/01773

Claims 1 and 6 are rejected under 35 U.S.C. § 102(b) in view of WO 89/01773 (Johnson *et al.*). The Office Action states Johnson *et al.* teaches the sequence N_Geneseq_032802, Accession AAN91262/c, which is a sequence of 34 bases having bases 8 to 20 of SEQ ID NO: 17 from the instant application.

In response, Applicants have amended claim 1 to now read on an oligonucleotide sequence from 15 to about 26 nucleotides in length. The Office Action identifies a 13 base pair sequence having sequence identity to SEQ ID 17. Because cited art no longer describes all of the elements of claim 1, it is no longer anticipatory.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection of claims 1 and 6 under 35 U.S.C. § 102(b).

Claims 1 and 6 are rejected in the alternative under 35 U.S.C. § 103(a) in view of WO 89/01773.

The legal determination under 35 U.S.C. § 103 is whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made. *In re O'Farrell*, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

As noted *supra*, Applicants have amended claim 1 to now read on an oligonucleotide sequence from 15 to about 26 nucleotides in length. Thus, Applicants' oligonucleotides are shorter than the sequence cited in the Office Action. Applicants aver that the cited reference does not provide a suggestion or motivation to select the specific oligonucleotides that are now claimed.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection of claims 1 under 35 U.S.C. § 103(a). In addition, this rejection has been rendered moot as to claims 4 and six, which have been cancelled.

C) Rejection of Claims 1, 4 and 6 Under 35 U.S.C. § 102(b) or in the alternative Under 35 U.S.C. § 103(a) in view of U.S. Patent No. 5,789,564

Claims 1, 4 and 6 are rejected under 35 U.S.C. § 102(b) in view of U.S. Patent No. 5,789,564 (hereinafter the '564 patent). The Office Action states that sequence 19 from the '564 patent teaches a sequence of 29 bases having bases 7, and 9-20 of SEQ ID NO: 17 of the instant application.

In response, Applicants have amended claim 1 to now read on an oligonucleotide sequence from 15 to about 26 nucleotides in length. The Office Action identifies 13 noncontiguous bases having sequence identity to SEQ ID NO. 17. Thus, this oligonucleotide is actually a mismatch oligonucleotide compared to SEQ ID NO. 17. Applicants note that mismatch oligonucleotides are used in the instant application as negative controls. Thus, the mismatch oligonucleotide of the '564 patent would not inherently have the properties of the claimed oligonucleotides.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection of claims 1, 4 and 6 under 35 U.S.C. § 102(b).

Claims 1, 4 and 6 are rejected in the alternative under 35 U.S.C. § 103(a) in view of U.S. Patent No. 5,789,564.

As noted *supra*, Applicants have amended claim 1 to now read on an oligonucleotide sequence from 15 to about 26 nucleotides in length. Thus, Applicants' oligonucleotides are shorter than the sequence cited in the Office Action. Applicants aver that the cited reference does not provide a suggestion or motivation to select the specific oligonucleotides that are now claimed. This rejection has been rendered moot as to claims 4 and 6, which have been cancelled.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection of claims 1, 4 and 6 under 35 U.S.C. § 103(a).

D) Rejection of Claims 1 and 6 Under 35 U.S.C. § 102(b) or in the alternative Under 35 U.S.C. § 103(a) in view of U.S. Patent No. 5,569,586

Claims 1 and 6 are rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,569,586 (hereinafter the '586 patent). The Office Action states that sequence 22 of the '586 patent is 32 bases in length, having bases 7 to 20 of SEQ ID NO: 18 of the instant application.

In response, Applicants have amended claim 1 to now read on an oligonucleotide sequence from 15 to about 26 nucleotides in length. The Office Action identifies a sequence having 14 bases of identity to SEQ ID NO: 18. Because cited art no longer describes all of the elements of claims 1, it is not anticipatory. This rejection is rendered moot as to claim 6, which has now been cancelled.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection of claims 1 and 6 under 35 U.S.C. § 102(b).

Claims 1 and 6 are rejected in the alternative under 35 U.S.C. § 103(a) as being obvious in view of U.S. Patent No. 5,569,586.

As noted *supra*, Applicants have amended claim 1 to now read on an oligonucleotide sequence from 15 to 26 nucleotides in length. Thus, Applicants' oligonucleotides are shorter than the sequence cited in the Office Action. Applicants aver that the cited reference does not provide a suggestion or motivation to select the specific oligonucleotides that are now claimed.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection of claims 1 and 6 under 35 U.S.C. § 103(a).

E) Rejection of Claim 7 Under 35 U.S.C. § 102(a) in view of WO 00/71703

Claim 7 is rejected under 35 U.S.C. § 102(a) in view of WO 00/71703 (International Publication Date of November 30, 2000). The Office Action states that sequence 1 from WO 00/71703 is 100% identical to SEQ ID NO: 17 of the instant application.

As indicated *supra*, Applicants have established that SEQ ID NO: 17 is entitled to a priority date of March 24, 2000. Therefore, WO 00/71703 cannot anticipate SEQ ID NO: 17.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection.

F) Rejection of Claim 7 Under 35 U.S.C. § 102(a) in view of WO 00/23112

Claim 7 is rejected under 35 U.S.C. § 102(a) in view of WO 00/23112 (International Publication Date of April 27, 2000). The Office Action states that WO 00/23112 teaches two sequences that are 100% identical to SEQ ID NOS: 17 and 18 of the instant application.

As indicated *supra*, Applicants have established that SEQ ID NOS: 17 and 18 are entitled to a priority date of March 24, 2000. Therefore, WO 00/23112 cannot anticipate SEQ ID NOS: 17 and 18.

Applicants respectfully request reconsideration and withdrawal of the outstanding rejection.

G) Rejection of Claims 1-6 Under 35 U.S.C. § 103(a) in view of Yoshida *et al.* and Others

Claims 1-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yoshida et al. in view of the collection of Taylor *et al.*, (DDT vol. 4, No. 12, 12/12/99, pages 562-567), Bennet *et al.*, (Chapter 2, pages 13-46, from Methods in Molecular Medicine: Antisense Therapeutics, 1996) Baracchini et al. (U.S. Patent No. 5,801,154), Cowsert (U.S. Patent No. 5,951,455), and the sequence of HDAC-1 (GenBank Accession No. U50079).

Applicants respectfully traverse this rejection. Due to differences in secondary structure and even chromatin structure, not all genes can be successfully inhibited by antisense oligonucleotides. Only Applicants' specification provides the requisite expectation of success. In addition, the requisite motivation to combine the cited references is missing. Yoshida et al. teaches that small molecule inhibitors of HDAC-1 are perfectly adequate to explore the function of HDAC. One skilled in the art would thus not be motivated by Yoshida et al. to seek out papers describing antisense experimentation.

6. CONCLUSION

It is believed that all of the objections and rejections raised in the outstanding Office Action have been addressed, and the amendments and remarks provided herewith have resolved all out-standing issues in the prosecution of the captioned application. Applicants respectfully request allowance of the currently pending claims.

Please charge any additional fees or credit any overpayment associated with this matter to our Deposit Account No. 50-2285.

Dated: 11/06/02

Respectfully submitted,

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MARKED-UP VERSION OF AMENDMENTS IN ACCORDANCE WITH 37 C.F.R. § 1.121
U.S.S.N. 09/817,538

1. (Amended) An oligonucleotide having nucleotide sequence of from [about 13] 15 to about [35] 26 nucleotides that inhibits one or more specific histone deacetylase isoforms, but less than all histone deacetylase isoforms, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA that encodes a portion of HDAC-1 (SEQ. ID NO: 2). [one or more histone deacetylase isoforms selected from the group consisting of:

(a) a nucleic acid molecule encoding a portion of HDAC-1 (SEQ ID NO: 2)[,

(b) a nucleic acid molecule encoding a portion of HDAC-2 (SEQ ID NO: 4),

(c) a nucleic acid molecule encoding a portion of HDAC-3 (SEQ ID NO: 6),

(d) a nucleic acid molecule encoding a portion of HDAC-4 (SEQ ID NO: 8),

(e) a nucleic acid molecule encoding a portion of HDAC-5 (SEQ ID NO: 10),

(f) a nucleic acid molecule encoding a portion of HDAC-6 (SEQ ID NO: 12),

(g) a nucleic acid molecule encoding a portion of HDAC-7 (SEQ ID NO: 14), and

(h) a nucleic acid molecule encoding a portion of HDAC-8 (SEQ ID NO: 16).]

PENDING CLAIMS

U.S.S.N. 09/817,538

1. (Amended) An oligonucleotide having nucleotide sequence of from 15 to about 26 nucleotides that inhibits one or more specific histone deacetylase isoforms, but less than all histone deacetylase isoforms, wherein the oligonucleotide is complementary to a region of RNA or double-stranded DNA that encodes a portion of HDAC-1 (SEQ ID NO: 2).

2. The oligonucleotide according to claim 1, wherein the oligonucleotide is a chimeric oligonucleotide.

3. The oligonucleotide according to claim 1, wherein the oligonucleotide is a hybrid oligonucleotide.

4. CANCELLED.

5. The oligonucleotide according to claim 1 having one or more phosphorothioate internucleoside linkage, being 20-26 nucleotides in length, and being modified such that the terminal four nucleotides at the 5' end of the oligonucleotide and the terminal four nucleotides at the 3' end of the oligonucleotide each have 2'-O-methyl groups attached to their sugar residues.

6. CANCELLED.

7. The oligonucleotide according to claim 6 that is SEQ ID NO: 17 or SEQ ID NO: 18.

8-36 CANCELLED.

Applicant

SHEET 1 OF 1

Subt. Form PTO-1449

SUPPLEMENTAL INFORMATION DISCLOSURE IN AN APPLICATION

(Use several sheets if necessary)

Docket Number	Application Number
MET-021US1	09/8[illegible]

Applicant: Li et al.

Filing Date	Group Art Unit
03/26/01	1645

U.S. PATENT DOCUMENTS

EXAMINER INITIAL	IDENTIFIER	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL	IDENTIFIER	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO
mms	B1	WO97/35990	10/02/97	PCT				
mms	B2	WO00/71703	11/30/00	PCT				
mms	B3	WO00/23112	04/27/00	PCT				
mms	B4	WO01/70675	09/27/01	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

EXAMINER INITIAL	IDENTIFIER	
mms	C9	Zhao et al. (1996), "Effect of Difference Chemically Modified Oligodeoxynucleotides on Immune Stimulation," 51 *Biochem. Pharmacol.* 2:173-182.
~~mms~~	~~C10~~	~~International Search Report of PCT/US01/09651~~

EXAMINER: M Schmidt	DATE CONSIDERED: 7/28/02

EXAMINER: Initial if citation is considered, whether or not citation is in conformance with MPEP §609; Draw line through citation if not in conformance and not considered. Include copy with next communication to Applicant.

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•Subt. For, PTO-1449

INFORMATION DISCLOSURE IN AN APPLICATION

(Use several sheets if necessary)

Sheet	1	OF	1

Docket Number	Application Number
106101.144	09/817,538

Applicant: Li et al.

Filing Date	Group Art Unit
03/26/2001	1643

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U.S. Patent Documents

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

Foreign Patent Documents

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

Other Documents (Including Author, Title, Date Pertinent Pages, Etc.)

MMS	A1	Yoshida M et al., "Potent and specific inhibition of mammalian histone deacetylase both in vivo and in vitro by trichostatin A" J Biol Chem. 1990 Oct 5;265(28):17174-9.
MMS	A2	Taunton J et al., "A mammalian histone deacetylase related to the yeast transcriptional regulator Rpd3p" Science. 1996 Apr 19;272(5260):408-11.
MMS	A3	Yoshida M et al., "Effects of trichostatins on differentiation of murine erythroleukemia cells" Cancer Res. 1987 Jul 15;47(14):3688-91.
MMS	A4	Sanchez del Pino MM "Properties of the yeast nuclear histone deacetylase" Biochem J. 1994 Nov 1;303 (Pt 3):723-9.
MMS	A5	Hu E et al., "Cloning and characterization of a novel human class I histone deacetylase that functions as a transcription repressor" J Biol Chem. 2000 May 19;275(20):15254-64.
MMS	A6	Kao HY et al., "Isolation of a novel histone deacetylase reveals that class I and class II deacetylases promote SMRT-mediated repression" Genes Dev. 2000 Jan 1;14(1):55-66.
MMS	A7	Grozinger CM et al., "Three proteins define a class of human histone deacetylases related to yeast Hda1p" Proc Natl Acad Sci U S A. 1999 Apr 27;96(9):4868-73.
MMS	A8	Csordas A et al., "On the biological role of histone acetylation" Biochem J. 1990 Jan 1;265(1):23-38

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EXAMINER	DATE CONSIDERED
M Schmidt	7/28/02

EXAMINER: Initial if citation is considered, whether or not citation is in conformance with MPEP § 609: Draw Line through citation if not conformance and not considered. Include copy with next communication to applicant.